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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,633	11/09/2001	Chien Ho	002547/20118/div2	5945

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EXAMINER

CARLSON, KAREN C

ART UNIT PAPER NUMBER

1653

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/986,633	<b>Applicant(s)</b> HO ET AL.	
	<b>Examiner</b> Karen Cochran Carlson, Ph.D.	<b>Art Unit</b> 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12, 13 and 15-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 12 is/are allowed.
- 6) ☒ Claim(s) 13 and 15-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2 IDSs</u> | 6) <input type="checkbox"/> Other: _____                                    |

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Claims 1-11, 13, 14, and 18-37 have been canceled. Claims 12, 13, and 15-17 are currently pending and under examination.

After review of the electronic file, it is noted that Applicants state that they have submitted the oath from parent application 09/598,218. However, the oath does not appear to be in the electronic file. Please re-submit the oath in response to this Office Action.

The disclosure is objected to because of the following informalities: The priority data should be updated. For example:

--This application is a divisional application of SN 09/598,216, filed June 21, 2000, now U.S. Patent 6, 486,123.---

Appropriate correction is required.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 13 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 6 of prior U.S. Patent No. 6,486,123. This is a double patenting rejection.

It is noted that instant Claim 13 refers to a nucleic acid sequence SEQ ID NO: 5 instead of an amino acid sequence encoding the beta chain. However, once this minor issue is addressed, the claims are identical, word for word.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that SEQ ID NO: 5 is a nucleic acid sequence and therefore cannot describe the hemoglobin beta-chain protein amino acid sequence, or provide basis for amino acid residue at position 108 of the beta chain. Therefore, because all claims recite or depend from a claim reciting SEQ ID NO:5 the claims are indefinite.

Indeed, no amino acid sequence is provided that depicts the amino acid sequence of human beta chain. Applicants should submit the sequence and comply with the sequence rules again in response to this Office Action, being careful not to add new matter by pointing out where in the specification the sequence is disclosed, in a cited reference, for example.

The closest prior art of record is the substitution of Asn  $\beta$  108 with either Lys or with Asp. See Hoffman et al. (USP 5,028,588), Moo-Penn et al. (1978; FEBS Letts 92:53-56), and O'Donnell et al. (1994; J. Bio. Chem. 269(44): 27692-27699), for example. These are non-conservative amino acid substitutions that result in the hemoglobin having lower oxygen affinity. The instant mutation of Asn  $\beta$  108 Gln is a conservative amino acid substitution. Conservative amino acid substitutions are generally considered by those skilled in the art to retain structure and function, and therefore one skilled in the art would not expect that the substitution of Asn  $\beta$  108 Gln would alter oxygen affinity. Additional reference is made to MPEP 2144.08(II)(4)(c):

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(c) Consider the Teachings of Structural Similarity. Consider any teachings of a "typical," "preferred," or "optimum" species or subgenus within the disclosed genus. If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *Deuel*, 51 F.3d at 1558, 34 USPQ2d at 1214 ("Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."). ..... **In the area of biotechnology, an exemplified species may differ from a claimed species by a conservative substitution ("the replacement in a protein of one amino acid by another, chemically similar, amino acid . . . [which] is generally expected to lead to either no change or only a small change in the properties of the protein."** *Dictionary of Biochemistry and Molecular Biology* 97 (John Wiley & Sons, 2d ed. 1989)). The effect of a conservative substitution on protein function depends on the nature of the substitution and its location in the chain. Although at some locations a conservative substitution may be benign, in some proteins only one amino acid is allowed at a given position. For example, the gain or loss of even one methyl group can destabilize the structure if close packing is required in the interior of domains. *James Darnell et al., Molecular Cell Biology* 51 (2d ed. 1990). The closer the physical and chemical similarities between the claimed species or subgenus and any exemplary species or subgenus disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner to the genus. See, e.g., *Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (and cases cited therein). Cf. *Baird*, 16 F.3d at 382-83, 29 USPQ2d at 1552 (disclosure of dissimilar species can provide teaching away).

The MPEP recognizes that conservative amino acid substitutions are obvious and not expected to impact function. The MPEP also recognizes that structural relationships provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. However, Applicants have provided the unexpected result that the conservative amino acid substitution at Asn  $\beta$  108 of hemoglobin lowers oxygen affinity, and this result was not predictable. Therefore, the claimed hemoglobin mutant is novel over the art of record.

Claims 15-17 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.


Claim 12 is allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A handwritten signature in black ink that reads "Karen Cochrane Carlson Ph.D." The signature is written in a cursive, flowing style.

KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER